REMARKS

Claims 53-64 are currently pending in this application. Claims 53 and 58 have been amended. Claims 54, 59 and 64 have been canceled. No new matter has been added in that the amended claims now recite the limitations of the canceled claims. In view of these amendments and of the following remarks, Applicants believe that all the asserted rejections are in condition for withdrawal and all the claims are in condition for allowance.

Claims 53-63 stand rejected under 35 U.S.C. 103(a) for purported unpatentability over Takami et al. The Examiner asserts that Takami et al. teach a composition containing 4-6 g of lysine and 4-7 g of arginine in a 100 ml parenteral solution.

The claimed invention inheres in administering a composition containing a combination of two specific amino acids to a patient in well-defined amounts in order to inhibit renal uptake of proteins and peptides that may be damaging to the patient's kidneys, without causing serious side effects to the patient. The novel finding of the present invention is that the administration of a combination of lysine and arginine show a synergistic effect that is more effective than both compounds alone at equimolar concentrations in inhibiting renal uptake of proteins and peptides that may damage the kidneys, and thus lower doses of the two amino acids can be used to effectively inhibit the renal uptake, and serious side effects, such as hyperkalemia, with associated vomiting, and cardiotoxicity is prevented.

The composition of the present invention has been studied and compared to prior art amino acid compositions in a number of patients. For example, comparative Example 4 describes a study that investigated the effect of a prior art "cocktail" of various amino acids administered to 26 patients. The results showed that a 4 hour infusion of 2030 ml of a 124.5 g cocktail of amino acids (Aminosteril N-Hepa) produced one or more episodes of moderate to severe vomiting in 42% of the patients. In contrast, working Example 6 describes a study that investigated the effect of a 25 g lysine and 25 g arginine composition administered to 11 patients. The results showed that after a 4 hour,

1000 ml infusion of the 50 g lysine/arginine composition, only one person experienced vomiting, which probably was caused by nausea that was present before the start of the infusion. Thus, it is clear from comparative Example 4 that serious side effects occur when a cocktail of various amino acids are administered to patients in amounts typically used in the prior art.

Based on the above, Applicants submit that the cocktail disclosed by Takami et al., e.g., as described in Example 1, if administered in a quantity that corresponds with the lower limit of arginine of the claimed invention, i.e., 15 g, a total quantity of approximately 220 g of amino acids would be administered to a patient, which would induce even greater serious side effects than the prior art cocktail described in comparative Example 4 of the present application, which administered a cocktail of 124.5 g of various amino acids.

Furthermore, Takami et al. describe animal experiments in which their cocktail of amino acids is administered to rats. Indeed, they only have administered their cocktail of amino acids to one individual. It is well known in the art that the observance of side effects, such as hyperkalemia, vomiting and cardiotoxicity, is patient-dependent, and thus the absence of side effects in this one individual disclosed by Takami et al. can be attributed to this patient-dependency, i.e., variability. Thus, if Takami et al. had administered their cocktail of amino acids to more than just one individual, as was done in comparative Example 4 of the present invention, there is no doubt that the same serious side effects would have been observed in a large percentage of those individuals.

Applicants therefore submit that the Takami et al. disclosure does not teach or suggest administering to a patient a combination of two specific amino acids, e.g., lysine and arginine, which show a surprising synergistic effect and thus lower doses of the two amino acids can be administered, which is capable of inhibiting renal uptake of protein and peptides that may damage the kidneys.

Claims 53-64 stand rejected under 35 U.S.C. 103(a) for purported unpatentability over Zaloga et al. The Examiner asserts that Zaloga et al. teach lysine

and arginine as useful in impairing the absorption of protein in kidney and treating renal failure.

In contrast to the claimed invention, which relates to the administration of a combination of only two specific amino acids to a patient in order to inhibit renal uptake of proteins and peptides that may be damaging to the kidneys, Zaloga et al. disclose nutritional compositions to prevent or recover from renal diseases or renal failure which include source protein, peptides and other substances, in addition to eleven amino acids, two of which happen to be lysine and arginine. For example, a nutritional composition is described which includes, per liter, 105 g protein, containing 7.5 g arginine and 5 g lysine, as well as nine other amino acids; 20 g casein or whey; 20 g beef; 7.7 g carnosine; 120 g carbohydrate; and 40 g fat. Thus, Zaloga et al. disclose a method for treating acute renal disease and renal failure by administering a nutritional composition containing a plurality of amino acids, a bulk of undefined protein, such as casein, beef and carnosine, carbohydrates and fat. Applicants submit that the above disclosure would not motivate one skilled in the art to practice the claimed invention.

In conclusion, neither Takami et al. nor Zaloga et al., alone or in combination, teach or suggest the new and unexpected findings of the method and therapeutic composition of the claimed invention, i.e., that the administration to a patient of a combination of two specific amino acids, e.g., lysine and arginine, which together show a surprising synergistic effect when combined, and thus lower doses of the two specific amino acids are needed which avoids serious side effects, is capable of inhibiting renal uptake of protein and peptides that may be damaging to the kidneys.

For all the foregoing reasons, claims 1-53, 55-58 and 60-63 are patentable over the cited prior art and in condition for allowance. Reconsideration of the rejections and allowance of pending claims claims 1-53, 55-58 and 60-63 are respectfully requested.

Respectfully submitted,

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